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4743 7590 01/22/2009 MARSHALL, GERSTEIN & BORUN LLP 233 SOUTH WACKER DRIVE 6300 SEARS TOWER CHICAGO, IL 60606-6357			EXAMINER FLOOD, MICHELE C	
			ART UNIT 1655	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/664,468

Applicant(s)

BAGCHI, DEBASIS

Examiner

Michele Flood

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 03 October 2008.
2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 51-83 is/are pending in the application.
4a) Of the above claim(s) 54-70 is/are withdrawn from consideration.
5) ☐ Claim(s) _____ is/are allowed.
6) ☒ Claim(s) 51-53 and 71-83 is/are rejected.
7) ☐ Claim(s) _____ is/are objected to.
8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-8508)
Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on October 3, 2008 has been entered.

Claims 51-53 and 71-83 are under examination.

Response to Arguments

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 52-53 and 71-83, as amended, are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims are rejected for failing to provide prior support or antecedent basis for the language "bilberry (*Vaccinium bracteatum*, *Vaccinium*

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caespitosum, *Vaccinium deliciosum*) extract" in Claims 51, 71, 72, 75, 76, 79, 80 and 83. Newly applied as necessitated by amendment.

Claim 51, as set forth in the amendment filed on October 3, 2008, now recites "A composition comprising two or more berry extracts selected from the group consisting of blueberry (*Vaccinium* L) extract, bilberry (*Vaccinium bracteatum*, *Vaccinium caespitosum*, *Vaccinium deliciosum*) extract, cranberry extract, elderberry extract, raspberry extract and strawberry extract, wherein the composition has a higher antioxidant capacity than any one berry extract used in the composition.

Claim 72, as set forth in the amendment filed on October 3, 2008, now recites "A composition comprising two or more berry extracts selected from the group consisting of blueberry (*Vaccinium* L) extract, bilberry (*Vaccinium bracteatum*, *Vaccinium caespitosum*, *Vaccinium deliciosum*) extract, raspberry extract and strawberry extract, wherein the composition has a higher antioxidant capacity than any one berry extract used in the composition."

Claim 80, as set forth in the amendment filed on October 3, 2008, now recites "A composition comprising two or more berry extracts selected from the group consisting of wild blueberry (*Vaccinium* L) extract, wild bilberry (*Vaccinium bracteatum*, *Vaccinium caespitosum*, *Vaccinium deliciosum*) extract, raspberry seed extract and strawberry extract, wherein the composition has a higher antioxidant capacity than any one berry extract used in the composition. the limitation

However, the specification as originally filed provides only for compositions comprising wild berry extract. Nowhere in the specification as originally filed does Applicant disclose a composition comprising a bilberry extract wherein the bilberry extract is any of the claim-designated species of *Vaccinium*. While it was indicated in the previous Office action that the metes and bounds of Claims 51, 71, 72, 75, 76, 79, 80 and 83 with particular regard to the terms "wild blueberry" and "wild bilberry, are uncertain because it is unclear as to the identification of the ingredients to which Applicant intends to direct the subject matter and that the standard Latin genus-species name of each ingredient should accompany non-technical nomenclature as a means for identifying the subject botanical noted in this application, it was not meant to direct Applicant to amend the claims to introduce new matter into the instantly claimed inventions. Thus, this is not a sufficient reason for Applicant to amend the claims to encompass subject matter disclosed in the as-filed specification. Applicant was not intentionally misguided. Moreover, while Applicant has amended the claims to encompass subject matter comprising the new concept of compositions comprising the claim-designated *Vaccinium sp.*, the Office notes that Applicant has not distinguished a bilberry extract from a "wild bilberry extract". Moreover, the Office notes that Applicant has not distinguished a "blueberry extract" from a "wild blueberry extract" or any other species of *Vaccinium*, given that the claims have been amended to only recite a "blueberry (*Vaccinium L.*) extract with regard to either a blueberry extract or a wild blueberry extract. As such both "bilberry extract" and "wild bilberry extract" are one and the

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same and not distinguished as one bilberry extract from the other, or even a blueberry extract, given Applicant's amendment to the claims. Thus, the original concept of the invention has been narrowed to encompass compositions comprising wild bilberry extract, wherein the wild bilberry is any of bilberry (*Vaccinium bracteatum*, *Vaccinium caespitosum*, *Vaccinium deliciosum*) extract.

Insertion of the above mentioned claim limitation has no support in the as-filed specification. The insertion of the limitation is a new concept because it neither has literal support in the as-filed specification by way of generic disclosure, nor are there specific examples of the newly limited genus which would show possession of the aforementioned broadened concept. There are only exemplified compositions comprising bilberry extract or wild bilberry extract. This is not sufficient support for the new genus. This is a matter of written description, not a question of what one of skill in the art would or would not have known. The material within the four corners of the as-filed specification must lead to the generic concept. If it does not, the material is new matter. Declarations and new references cannot demonstrate the possession of a concept after the fact. Thus, the insertion of the above mentioned claim limitation is considered to be the insertion of new matter for the above reasons.

As the above mentioned claim limitation could not be found in the present specification, the recitation of the claim limitation is deemed new matter; and, therefore it must be omitted from the claim language, unless Applicant can particularly point to the specification for literal support.

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The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 51-53 and 71-83, as amended, remain rejected under 35

U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The rejection remains the same for the reason set forth in the previous Office action and for the reason set forth herein.

Claim 51, 71, 72, 76, 75, 76, 79, 80 and 83, as amended, remain vague and indefinite by the term "extract" because this term, in and of itself, does not adequately delineate its metes and bounds. This term is best defined as a product-by-process since product-by-process claims are intended to define products which are otherwise difficult to define (and/or distinguish from the prior art). For example, is the extract obtained via extraction with water, a polar solvent, a non-polar solvent, an acid or base, a squeezed extract, or something else? In addition, from what part(s) of the plant is the extract obtained? It is well accepted in the herbal art that extraction with one of various distinct solvents, as well as from particular parts of therapeutic plants, has a profound impact on the final product with respect to the presence, absence, amounts, and/or ratios of active ingredients therein and, thus, its ability to provide the desired functional effect(s) instantly claimed and/or disclosed. Since the extract itself is clearly essential to the claimed invention, the step(s) by which the claimed extract is obtained are also clearly essential and, therefore, must be recited in the claim language itself (i.e., as a product-by-process). Please note that although the

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claims are interpreted in light of the specification, critical limitations from the specification cannot be read into the claims (see, e.g., *In re Van Guens*, 988 F.2d 1181, 26 PSPG2d 1057 (Ded. Cir. 1991)). Accordingly, without the recitation of all these critical limitations as set forth above, the claims do not adequately define the instant invention.

Applicant argues that consistent with the disclosure of the specification, as well as the Declaration of Dr. Debasis Bagchi filed January 25, 2007, one of ordinary skill in the art would understand the meaning of the term "berry extract" as an aqueous alcohol extract of a berry. Applicant's argument has been fully considered. However, it is unclear as to how Applicant has arrived to this conclusion without supporting documentation teaching or suggesting Applicant's definition of the term "berry extract". Furthermore, the subject matter of Claims 76-83 encompasses compositions comprising "two or more berry extracts" comprising a raspberry seed extract. Given the foregoing and given that the claims are set forth only in terms of a composition comprising two or more berry extracts wherein the berry extract is defined only in terms of a genus species or the plant name itself, one of ordinary skill in the art would reasonably read the claims as reciting a composition comprising a berry extract prepared by no particular solvent and any and all parts thereof a berry-bearing plant. Thus, while Applicant's arguments have been fully considered the rejection remains the same for the reason set forth in the previous and the reason set forth herein.

The metes and bounds of Claims 71, 75, 79 and 83 remain rendered uncertain because the percentage amounts of the ingredients are not set forth in

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terms of either "by weight" or "by volume" percentage amount based on the total amount of the composition. The lack of clarity renders the claims indefinite since the resulting claims do not clearly set forth the metes and bounds of the patent protection desired. Applicant argues the rejection should be withdrawn because the claims do set forth that the percent amounts are "by weight". Applicant's argument has been fully considered but is not persuasive because the claims are not set forth in terms of weight percentage amount based on the total weight of the composition.

All other cited claims depend directly or indirectly from rejected claims and are, therefore, also, rejected under U.S.C. 112, second paragraph for the reasons set forth above.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 51-53, 722-74, 76-78 and 80-82, as amended, remain rejected under 35 U.S.C. 102(b) as being anticipated by Powrie et al. (A*), as evidenced by the teachings of Shanbrom (B), Ou et al. (C*), Wang et al. (U) and Mann (D*). Applicant's arguments have been fully considered. However, the rejection

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remains for the reason set forth herein and for the reason set forth in the previous Office action and repeated immediately below.

At [0160], Powrie teaches a composition comprising concentrated cranberry juice (read herein as a cranberry extract); concentrated blueberry juice (read herein as either a blueberry extract or wild blueberry extract); and black raspberry juice (read herein as a raspberry seed extract, since Powrie does not teach separating the seeds from the fruit).

Powrie does not expressly teach that the reference composition has an oxygen radical capacity above 40 Trolox equivalents/gram fresh weigh basis. However, the composition taught by Powrie comprises one and the same ingredients disclosed by Applicant as having the claim-designated property. Therefore, an oxygen radical capacity above 40 Trolox equivalents/gram fresh weigh basis is considered inherent to the composition taught by Powrie, absent clear and convincing evidence to the contrary.

Moreover, as evidenced by the teachings of Shanbrom at [0025], cranberry, blueberry and raspberry juices have high antioxidant capacity. For example, Ou teaches that the ORAC value of blueberry juice is 3.16 and that the ORAC value of raspberry juice is 2.34, wherein the ORAC values are expressed as micromole Trolox equivalent per liter ($n > 3$). See Table 2. According to Wang, for fresh black raspberry fruits ORAC values range from 16.1 \pm 0.6 to 33.7 \pm 4.0. See Table 2. Finally, Mann teaches that cranberry juice has a ORAC value of 0.007.

Applicant argues that Powrie fails to anticipate the claimed invention 'because Powrie teaches juice compositions and not berry extracts.' Thereby, Applicant asserts that the Powrie' juice compositions would not inherently have the claimed antioxidant capacities. Applicant further argues that Ou teaches away from the claimed invention since Ou teaches that extracts ("similar to the claimed invention") such as bilberry and elderberry extracts have low oxygen radical capacities (about 2-3 Trolox equivalents/gram⁻¹). Applicant's arguments have been fully considered. However, they are neither persuasive nor commensurate in scope to the instantly claimed invention. As presently drafted, the claims encompass subject matter directed to compositions comprising two or more berry extracts. The juices taught by Powrie are compositions extracted from berries. Thus, the Powrie' juices are berry extracts. The extraction of juices absent separation of the seed from either the skin or fresh pulp of a berry, such as the raspberry taught by Powrie and the claim-designated raspberry seed extract, are berry extracts containing a berry seed extract. Thus, the raspberry juice extract taught by Powrie is a raspberry seed extract. Therefore, given the broadest reasonable interpretation of the claims, Powrie teaches a composition comprising cranberry extract, blueberry extract or wild blueberry extract, and raspberry seed extract.(read herein as a raspberry seed extract, since Powrie does not teach separating the seeds from the fruit). Given that Powrie does not teach a composition comprising either bilberry or elderberry extracts and given the teachings as a whole, Applicant's arguments with regard to the Ou' reference is moot.

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The reference anticipates the claimed subject matter.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 51-53 and 72-74, as amended, are rejected under 35 U.S.C.

103(a) as being unpatentable over Joseph et al. (V) in view of Wang et al. (W) and Prior et al. (X). Newly applied.

Joseph beneficially teaches that dietary supplements of blueberry extract or strawberry extract fed to 8 weeks to 19-month old Fischer 344 rats were effective in reversing age-related deficits in several neuronal and behavioral parameters.

The teachings of Joseph are set forth above. Joseph does not teach a composition comprising blueberry extract and strawberry extract, wherein the composition has a higher antioxidant capacity than any one berry extract used in the composition or wherein the composition has a higher oxygen radical absorbance capacity than the oxygen radical absorbance capacity of any one berry extract used in the composition or wherein the composition has an oxygen radical absorbance capacity above 40 micromoles of Trolox equivalents (TE)/gm fresh weight basis. However, it would have been obvious to one of ordinary skill

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in the art to combine the blueberry extract and the strawberry extract taught by Joseph to provide the instantly claimed composition because at the time the invention was made Joseph taught, "Ample research indicates that age-related neuronal-behavioral decrements are the result of oxidative stress that may be ameliorated by antioxidants." See abstract. Per the teachings of Wang and Prior, Joseph also taught that blueberry extract and strawberry extract had been identified as being high in antioxidant activity via the oxygen radical absorbance capacity assay, on page 8114, Column 2, paragraph 2. For instance, in Table I, Wang measured the antioxidant capacity of strawberry fruit extract using the oxygen radical absorbance capacity (ORAC) assay with regard to the effect of acetone extraction time on ORAC (nanomoles of Trolox equivalents per gram) measured in fruit pulp, wherein the TEAC/g ranged from 847 ± 29 (2 min) to 1129 ± 113 (4h); and, Prior teaches that the Trolox equivalent antioxidant capacity of blueberry extracts (*Vaccinium* L.), as measured by ORAC, ranged from a low of 13.9 to 45.9 micromole TE/g of fresh berries, depending upon the maturity, the anthocyanin and total phenolic content and variety of the blueberry. See Table 1. Prior further taught, on the basis of wet weight (edible portion) that strawberry had a relatively high antioxidant capacity of $15.4 \mu\text{mol}$ Trolox equivalents (TE)/g of fresh weight. Moreover, Joseph observed that blueberry extract supplementation was more effective than strawberry extract supplementation in reversing age-related deficits related to functional neuronal indices, whereas strawberry supplementation primarily increased striatal muscarinic receptor sensitivity reflected in the reversal of cognitive behavioral deficits, and whereas

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both berry extract supplements improved the cognitive performance. At the time the invention was made, one of ordinary skill in the art would have been motivated to combine the blueberry extract and the strawberry extract taught by Joseph to provide the instantly claimed composition because Joseph observed that the berry extracts fed to rats were shown to be effective in reversing age-related deficits in several neuronal and behavioral parameters, including oxotremorine enhancement of K^+ -evoked release of dopamine from striatal slices, carbachol-stimulated GPTase activity, striatal Ca^{45} buffering in striatal synaptosomes, motor behavioral performance on the rod walking and acelerod tasks and water maze performance. Given the teachings as a whole, the artisan of ordinary skill made would have had a reasonable expectation that the combining of a blueberry extract and a strawberry extract would be a success in providing not only a composition having a higher antioxidant capacity than any one berry extract used in the composition and a higher oxygen radical absorbance capacity than the oxygen radical absorbance capacity than one berry extract used in the composition, such as the strawberry extract taught by either Wang or Prior; and having an oxygen radical absorbance capacity above 40 micromoles of Trolox equivalents (TE)/gram fresh weight basis, such as the high antioxidant capabilities of the blueberry extracts and strawberry extracts taught by Wang and Prior, but would also be a success in the making of a dietary supplement capable of mitigating the effects of oxidative stress implicated in the pathogenesis of neurodegenerative disease, as Joseph suggested that the results of his study indicate that the phytochemicals present in antioxidant-rich

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foods may be beneficial in reversing the course of neuronal and behavioral aging, in addition to their known beneficial effects on cancer and heart disease.

Moreover, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the claimed ingredients in the making of the claimed composition because it is well known that its *prima facie* obvious to combine two or more ingredients each of which is taught by the prior art to be useful for the same purpose in order to form a third composition which is useful for the same purpose. The idea for combining them flows logically from their having been used individually in the prior art. *In re Pinten*, 459 F. 2d 1053, 173 USPQ 801 (CCPA 1972); *In re Susi*, 58 CCPA 1074, 1079-80; 440 F.2d 442, 445; 169 USPQ 423, 426 (1971); *In re Crockett*, 47 CCPA 1018, 1020-21; 279 F.2d 274, 276-277; 126 USPQ 186, 188 (1960). For example, on page 2692, last paragraph of Column 2, Prior teaches, "Studies are continuing in our laboratory of the implications of consuming foods containing increased quantities of ORAC. The antioxidant rich phytochemicals in strawberries have been shown in rat models to reduce or retard the central nervous system deficits seen in aging [citation omitted] and to protect against the oxidative stress caused by 100% oxygen exposure [citation omitted]. Since the antioxidant capacity of blueberries is higher than for strawberries, a benefit of consuming antioxidants from blueberries would also be expected. Furthermore, consumption of a more concentrated source of antioxidants will have the greatest impact on in vivo antioxidant capacity. We have estimated that normal intake in humans of antioxidants as measured by ORAC within the U.S. is in the range of 1.2-1.7

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mmol ORAC/day [citation omitted]. Increases in serum ORAC are observed with intakes of 3-4 mmol Trolox equiv/day, and some individuals have been observed to have ORAC intakes as high as 6 mmol/day [citation omitted]. Consumption of ½ cup of blueberries (72.5) would increase ORAC intake by 1-3.2 mmol, depending upon the blueberry variety and maturity. Thus, the ORAC of the blueberry source can have marked effects of total daily ORAC intake." Thus, at the time the invention was one of ordinary skill in the art would have been motivated and one would have had a reasonable expectation of success to add the blueberry extract to the strawberry extract used in the method taught by Joseph to provide the instantly claimed composition because the claimed invention is no more than the combining of well known ingredients known for their beneficial functional effect to mitigate the effects of free radicals due to their high oxygen radical absorbance capacities and in general beneficial to health and contributing to the amelioration of degenerative processes in humans.

Based upon the beneficial teachings of the cited references, the skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Accordingly, the claimed invention was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, especially in the absence of evidence to the contrary.

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Claims 51-53, 72-74, 76-78 and 80-82 are rejected under 35 U.S.C. 103(a) as being unpatentable over Joseph et al. (V) in view of Wang et al. (W), Prior et al. (X) and Moyer et al. (U1). Newly applied.

Joseph beneficially teaches that dietary supplements of blueberry extract or strawberry extract fed to 8 weeks to 19-month old Fischer 344 rats were effective in reversing age-related deficits in several neuronal and behavioral parameters.

The teachings of Joseph are set forth above. Joseph does not teach a composition comprising blueberry extract and strawberry extract, wherein the composition has a higher antioxidant capacity than any one berry extract used in the composition or wherein the composition has a higher oxygen radical absorbance capacity than the oxygen radical absorbance capacity of any one berry extract used in the composition or wherein the composition has an oxygen radical absorbance capacity above 40 micromoles of Trolox equivalents (TE)/gm fresh weight basis. However, it would have been obvious to one of ordinary skill in the art to combine the blueberry extract and the strawberry extract taught by Joseph to provide the instantly claimed composition because at the time the invention was made Joseph taught, "Ample research indicates that age-related neuronal-behavioral decrements are the result of oxidative stress that may be ameliorated by antioxidants." See abstract. Per the teachings of Wang and Prior, Joseph also taught that blueberry extract and strawberry extract had been identified as being high in antioxidant activity via the oxygen radical absorbance capacity assay, on page 8114, Column 2, paragraph 2. For instance, in Table I,

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Wang measured the antioxidant capacity of strawberry fruit extract using the oxygen radical absorbance capacity (ORAC) assay with regard to the effect of acetone extraction time on ORAC (nanomoles of Trolox equivalents per gram) measured in fruit pulp, wherein the TEAC/g ranged from 847 ± 29 (2 min) to 1129 ± 113 (4h); and, Prior teaches that the Trolox equivalent antioxidant capacity of blueberry extracts (*Vaccinium* L.), as measured by ORAC, ranged from a low of 13.9 to 45.9 micromole TE/g of fresh berries, depending upon the maturity, the anthocyanin and total phenolic content and variety of the blueberry. See Table 1. Prior further taught, on the basis of wet weight (edible portion) that strawberry had a relatively high antioxidant capacity of $15.4 \mu\text{mol}$ Trolox equivalents (TE)/g of fresh weight. Moreover, Joseph observed that blueberry extract supplementation was more effective than strawberry extract supplementation in reversing age-related deficits related to functional neuronal indices, whereas strawberry supplementation primarily increased striatal muscarinic receptor sensitivity reflected in the reversal of cognitive behavioral deficits, and whereas both berry extract supplements improved the cognitive performance. At the time the invention was made, one of ordinary skill in the art would have been motivated to combine the blueberry extract and the strawberry extract taught by Joseph to provide the instantly claimed composition because Joseph observed that the berry extracts fed to rats were shown to be effective in reversing age-related deficits in several neuronal and behavioral parameters, including oxotremorine enhancement of K^+ -evoked release of dopamine from striatal slices, carbachol-stimulated GPTase activity, striatal Ca^{45} buffering in striatal

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synaptosomes, motor behavioral performance on the rod walking and acelerod tasks and water maze performance. Given the teachings as a whole, the artisan of ordinary skill made would have had a reasonable expectation that the combining of a blueberry extract and a strawberry extract would be a success in providing not only a composition having a higher antioxidant capacity than any one berry extract used in the composition and a higher oxygen radical absorbance capacity than the oxygen radical absorbance capacity than one berry extract used in the composition, such as the strawberry extract taught by either Wang or Prior; and having an oxygen radical absorbance capacity above 40 micromoles of Trolox equivalents (TE)/gram fresh weight basis, such as the high antioxidant capabilities of the blueberry extracts and strawberry extracts taught by Wang and Prior, but would also be a success in the making of a dietary supplement capable of mitigating the effects of oxidative stress implicated in the pathogenesis of neurodegenerative disease, as Joseph suggested that the results of his study indicate that the phytochemicals present in antioxidant-rich foods may be beneficial in reversing the course of neuronal and behavioral aging, in addition to their known beneficial effects on cancer and heart disease.

Moreover, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the claimed ingredients in the making of the claimed composition because it is well known that its *prima facie* obvious to combine two or more ingredients each of which is taught by the prior art to be useful for the same purpose in order to form a third composition which is useful for the same purpose. The idea for combining them flows logically from

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their having been used individually in the prior art. *In re Pinten*, 459 F. 2d 1053, 173 USPQ 801 (CCPA 1972); *In re Susi*, 58 CCPA 1074, 1079-80; 440 F.2d 442, 445; 169 USPQ 423, 426 (1971); *In re Crockett*, 47 CCPA 1018, 1020-21; 279 F.2d 274, 276-277; 126 USPQ 186, 188 (1960). For example, on page 2692, last paragraph of Column 2, Prior teaches, "Studies are continuing in our laboratory of the implications of consuming foods containing increased quantities of ORAC. The antioxidant rich phytochemicals in strawberries have been shown in rat models to reduce or retard the central nervous system deficits seen in aging [citation omitted] and to protect against the oxidative stress caused by 100% oxygen exposure [citation omitted]. Since the antioxidant capacity of blueberries is higher than for strawberries, a benefit of consuming antioxidants from blueberries would also be expected. Furthermore, consumption of a more concentrated source of antioxidants will have the greatest impact on in vivo antioxidant capacity. We have estimated that normal intake in humans of antioxidants as measured by ORAC within the U.S. is in the range of 1.2-1.7 mmol ORAC/day [citation omitted]. Increases in serum ORAC are observed with intakes of 3-4 mmol Trolox equiv/day, and some individuals have been observed to have ORAC intakes as high as 6 mmol/day [citation omitted]. Consumption of ½ cup of blueberries (72.5) would increase ORAC intake by 1-3.2 mmol, depending upon the blueberry variety and maturity. Thus, the ORAC of the blueberry source can have marked effects of total daily ORAC intake." Thus, at the time the invention was one of ordinary skill in the art would have been motivated and one would have had a reasonable expectation of success to add

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the blueberry extract to the strawberry extract used in the method taught by Joseph to provide the instantly claimed composition because the claimed invention is no more than the combining of well known ingredients known for their beneficial functional effect to mitigate the effects of free radicals due to their high oxygen radical absorbance capacities and in general beneficial to health and contributing to the amelioration of degenerative processes in humans.

Joseph is silent as to the variety of blueberry used in the making of the blueberry extract supplement for treating neuronal deficits. Thus, the references do not specifically teach a composition comprising a wild blueberry extract.

Moyer teaches the total anthocyanins and total phenolic contents and antioxidant capacities as determined by oxygen radical absorbing capacity (ORAC) of fruits of various blueberries (*Vaccinium* L.) in Table 1. Moyer teaches that both blueberry extract and wild blueberry extract have high ORAC values in terms of Trolox equivalents micromoles per gram on fresh weight basis, as well as high contents of anthocyanins and phenolics. Thus, it was known in the art at the time of the invention, that both blueberry extract and wild blueberry extract have high antioxidant capacity as measured by an oxygen radical absorbance capacity assay; and that the highest ORAC values observed in the blueberry (*Vaccinium* L.) population belonged to wild blueberry extract. For example, wild selections of rabbiteye blueberry, *Vaccinium ashei*, from Florida and Georgia had the highest ORAC (131, 129 and 122 $\mu\text{mol TE/g}$. See Table 1. Therefore, an artisan of ordinary skill would have had a reasonable expectation that using wild blueberry extract or blueberry extract having relatively high ORAC values would

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be useful in preparing a composition having the claim-designated physical parameters when combined with a strawberry extract as taught by either Wang or Prior. This reasonable expectation of success would have motivated the artisan to use the blueberry extract or wild blueberry extracts as taught by Moyer, given that Prior similarly teaches the similar blueberry cultivars having similar ORAC values as suggested by Joseph to prepare a blueberry extract for dietary supplementation to mitigate oxidative stress implicated in the pathogenesis of neurodegenerative diseases. Thus, at the time the invention was made, the instantly claimed invention would have been no more than a matter of judicial selection for one of ordinary skill in the art to pick and choose a blueberry extract having an antioxidant capacity higher than the strawberry extract taught by Wang and Prior to provide a result effect variable, since it was well established that blueberry extracts having high antioxidant capacity and high contents of anthocyanins and phenolics are beneficial in the making of dietary supplements due to their health promoting effects; and could augment the beneficial health promoting effects of the strawberry extract taught by the combined teachings.

Based upon the beneficial teachings of the cited references, the skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Accordingly, the claimed invention was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, especially in the absence of evidence to the contrary.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michele Flood whose telephone number is 571-272-0964. The examiner can normally be reached on 7:00 am - 3:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Terry McKelvey can be reached on 571-272-0775. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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January 18, 2009

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